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ning of each regular issue of the PCT Gazette.

WO 00/63364 A3

(54) Title: METHODS AND COMPOSITIONS FOR INHIBITING THE FUNCTION OF POLYNUCLEOTIDE SEQUENCES

(57) Abstract: A therapeutic composition for inhibiting the function of a target polynucleotide sequence in a mammalian cell includes an agent that provides to a mammalian cell an at least partially double-stranded RNA molecule comprising a polynucleotide sequence of at least about 200 nucleotides in length, said polynucleotide sequence being substantially homologous to a target polynucleotide sequence. This RNA molecule desirably does not produce a functional protein. The agents useful in the composition can be RNA molecules made by enzymatic synthetic methods or chemical synthetic methods *in vitro*; or made in recombinant cultures of microorganisms and isolated therefrom, or alternatively, can be capable of generating the desired RNA molecule *in vivo* after delivery to the mammalian cell. In methods of treatment of prophylaxis of virus infections, other pathogenic infections or certain cancers, these compositions are administered in amounts effective to reduce or inhibit the function of the target polynucleotide sequence, which can be of pathogenic origin or produced in response to a tumor or other cancer, among other sources.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/10555

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 C12N15/63 C12N15/70 C12N15/86 C07K14/01
C07K14/08 A61K48/00 A61K38/16 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MONTGOMERY M K ET AL: "Double-stranded RNA as a mediator in sequence-specific genetic silencing and co-suppression" TRENDS IN GENETICS,NL,ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, vol. 14, no. 7, 1 July 1998 (1998-07-01), pages 255-258, XP004124680 ISSN: 0168-9525 the whole document	1
X	WO 95 27783 A (JOSHI SUKHWAL SADNA) 19 October 1995 (1995-10-19) page 8, line 29 -page 11, line 10 -/-	1,4,5,8, 9,28, 32-40, 42-45, 48,55, 56,58, 61-63



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/10555

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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	PLAYER MARK R ET AL: "Targeting HIV mRNA for degradation: 2,5-A antisense chimeras as potential chemotherapeutic agents for AIDS." NUCLEOSIDES & NUCLEOTIDES, vol. 16, no. 7-9, July 1997 (1997-07), pages 1221-1222, XP000952972 ISSN: 0732-8311 the whole document	1,42-45
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/10555

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	YUKIKO TONE ET AL: "STRUCTURE AND CHROMOSOMAL LOCATION OF THE MOUSE INTERLEUKIN-12 P35 AND P40 SUBUNIT GENES" EUROPEAN JOURNAL OF IMMUNOLOGY, DE, WEINHEIM, vol. 26, no. 6, 1 June 1996 (1996-06-01), pages 1222-1227, XP000612644 ISSN: 0014-2980 cited in the application the whole document	1
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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>WIANNY F ET AL: "Specific interference with gene function by double-stranded RNA in early mouse development" NATURE CELL BIOLOGY, GB, MACMILLAN PUBLISHERS, vol. 2, no. 2, February 2000 (2000-02), pages 70-75, XP002138445 ISSN: 1465-7392 the whole document</p> <p>---</p>	1,3,6,8, 9
P, X	<p>WO 99 53050 A (WANG MING BO ; COMMW SCIENT IND RES ORG (AU); GRAHAM MICHAEL WAYNE) 21 October 1999 (1999-10-21) cited in the application</p> <p>page 1, line 1-17 page 8, line 5 -page 10, line 20 page 22, line 4 -page 23, line 2 page 26, line 1-25</p> <p>---</p>	1,3-6,8, 10-16, 35-40, 42, 61-63,65
E	<p>WO 00 44914 A (FARRELL MICHAEL J ; LI YIN XIONG (US); KIRBY MARGARET L (US); MEDIC) 3 August 2000 (2000-08-03) page 2, line 20 -page 5, line 10 page 10, line 4 -page 19, line 17; example III</p> <p>---</p>	1,3,6,8, 9,28,33, 34,42
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T	<p>PARK WEE-SUNG ET AL: "Inhibition of HIV-1 replication by a new type of circular dumbbell RNA/DNA chimeric oligonucleotides." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 270, no. 3, 21 April 2000 (2000-04-21), pages 953-960, XP002151277 ISSN: 0006-291X the whole document</p> <p>-----</p>	1,6,8, 42-45, 55,56, 58, 61-63,65

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1,42,46,48,49,52-63

Present claims 1,42,46,48,49 and 52-63 relate to an extremely large number of possible compounds (agents and/or target polynucleotides). In fact, the claims contain so many options that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear and concise, namely, (a) agents: partially ds-RNA, dsRNA, ss-RNA sense and antisense, circular RNA, lariats and hybrid RNA-DNA as mentioned in the description at pages 8, line 5 to page 9, line 4, and page 14, line 1 to page 16, line 22, and (b) target polynucleotides gag gene of HIV, the gD gene of HSV, type 2 genome and to a polynucleotide sequence homologous to IL-12p40 murine messenger RNA as recited in examples 1-4.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/10555

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